

**REMARKS**

The present invention relates to a method for the manufacture of a prothrombin time measuring reagent and to reagent made thereby.

In the Office Action of July 3, 2003, original claims 1-10 were rejected for indefiniteness under 35 U.S.C. § 112, with respect to certain terminology in claims 1, 4, 5, and 7. Claims 1-10 were also rejected under 35 U.S.C. § 102(b) based on GB 872,536 (GB '536) and also based on U.S. Patent 4,416,812 (US '812) or based on U.S. Patent 5,270,451 (US '451). Furthermore, claims 1-10 were rejected under 35 U.S.C. § 102(b) based on JP 06-337267 (JP '267) or Hardy et al.

In the present Amendment, Applicants have canceled the rejected claims 1-10 and submit herewith claims 11-28, which claims include improved wording to obviate the issues under 35 U.S.C. § 112 that were raised in the Office Action.

With respect to the several prior art rejections, Applicants respectfully submit that claims 11-28 herein are not anticipated under 35 U.S.C. § 102(b) by any of the five cited references relied upon for rejection, for the reasons explained below.

1. GB 872,536 (GB '536)

GB '536 does not include descriptions on thromboplastin, nor descriptions on prothrombin time measuring reagent. The present invention is directed specifically to prothrombin time measuring reagent. GB '536 only relates to how to purify blood coagulation factor, and describes adsorbing the factor with barium sulphate (page 2, lines 95-101), washing

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the barium sulphate (page 2, lines 102--103), and eluting the factor from the barium sulphate (page 2, lines 104-108). The prepared composition in the article is not identified as a prothrombin time measuring reagent, and is not described as being used for the purpose

In the new claims herein, selected amino acids are set forth for addition to a prothrombin time measuring reagent. Furthermore, Applicants note that glycine is not proper for controlling ISI.

2. U.S. Patent 4,416,812 (US '812)

In Example 4 of US '812, there is described thromboplastin reagent with added glycine. Such is not within the scope of the new claims herein.

3. U.S. 5,270,451 (US '451)

The disclosure of U.S. '451 is essentially similar to that of US '812, and the same comments as above apply.

4. JP 06-337267 (JP '267)

JP '267 describes a thrombotest with added amino acid such as sodium glutamate. However, this reagent is a reagent for measuring coagulation factor II, VI and X, which characteristically contain adsorbed plasma. Applicants note that the prothrombin time measuring reagent according to the present invention is a reagent for measuring coagulation factor II, VII,

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X, V and fibrinogen, which is different from the thrombotest of JP '267 in its composition and purpose of use.

5. Hardy article

Thrombokinase is an enzyme, which had been earlier supposed to be related to blood coagulation proceeding by cascade. It was supposed that blood coagulation proceeded by reaction of this enzyme and  $\text{Ca}^{++}$  ion. However, blood coagulation proceeds by action of many kind of blood coagulation factors.

Hardy's article simply describes shortcutting of prothrombin time by the mixing of glutamic acid and thrombokinase. However, the composition described in the Hardy article is different from the present invention's composition for prothrombin time measuring reagent and in its purpose of use. Hardy fails to disclose or suggest adding glutamic acid to prothrombin time measuring reagent. Furthermore, Applicants note that glutamic acid is not proper for controlling ISI.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

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The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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